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(54) Leukotriene antagonistic benzoic acid derivatives

(57) The invention relates to benzoic acid derivatives being leukotriene antagonists. The compounds therefore are suitable as active ingredients in medicaments particularly in medicaments for the treatment of respiratory diseases.

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Example 36

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5-aza-6-(5-carboxy-2-(3-[3-{4-phen xybutoxy}phenyl]pr p xy)phenyl)-6-oxohexanoic acid

10 CO₂H

This was prepared from 3-[3-{4-phenoxybutoxy}phenyl]propyl bromide and the product of Example 4a following the procedure of Examples 4b and 4c.

HPLC T_R: 4.1 min, 70:30:01.

Ester: ¹H-NMR (CDCl₃)δ: 1.8-2.2 (8H,m), 2.3 (2H,t)2.75 (2H,t), 3.45 (2H,t), 3.56 (3H,s), 3.8-4.3 (6H,m), 6.7-7.4 (10H,m), 7,8 (1H,m), 8.10 (1H,dd), 8.70 (1H,d).

Claims

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1. Benzoic acid derivatives of the formula (I)

40 (I)

where

R¹ represents hydrogen, alkyl having up to 6 carbon atoms or represents substituted phenyl,

P and Q each represent oxygen, sulfur or a bond,

X represents oxygen, sulfur or -CONH-,

T represents an ethylene group, oxygen, sulfur or a bond,

Y represents a group -COOH, -NHSO₂R³ or -CONHSO₂R³

55 wherein

R² denotes hydrogen, halogen, trifluoromethyl, trifluoromethoxy, nitro, cyano or denotes alkyl or alkoxy,

and

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		Z	represents a group of the formula -COOH, COR 4 , -CO(CH $_2$) $_p$ CO $_2$ H, -O(CH $_2$) $_p$ CO $_2$ H, -S(CH $_2$) $_p$ CO $_2$ H, NO $_2$, -CONHWCO $_2$ H or -NHWCO $_2$ H	
		wherein		
5		R ²	has the above mentioned meaning,	
10		\mathbb{R}^3	denotes trifluoromethyl, alkyl or optionally substituted phenyl,	
		R ⁴	represents a group of the formula WCO ₂ H or alkyl,	
		р	is an integer from 0 to 5 and	
15		w	denotes phenylene, an alkylene group having up to 8 carbon atoms, which is optionally substituted by alkyl or cycloalkyl each having up to 6 carbon atoms or denotes a group -CO(CH_2) _q - or -(CH_2) _q - where	
20		q	is an integer from 0 to 5	
		m	is an integer from 0 to 6	
		and		
25		n	is an integer from 0 to 4	
		and salts thereof.		
30	2.	Benzo where	enzoic acid derivatives of the formula according to Claim 1,	
		R ¹	represents hydrogen,	
35		P and	Q represent oxygen,	
		X	represents oxygen sulfur or -NH-,	
40		Т	represents a bond,	
		Υ	represents a group -COOH and/or	
		Z	has the abovementioned meaning	
45		m represents an integer H		
		and their salts.		
50	3.		Benzoic acid derivatives of the formula according to Claim 1, wherein	
		R ¹	represents hydrogen,	
55		P and	Q represent oxygen,	
		T	represents a bond,	
		X	represents oxygen,	

Y represents a group -COOH,

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m is an integer 4,

n is an integer 3

5 and

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- Z represents a group -CONH(CH₂)_qCO₂H, -NHCO(CH₂)_qCO₂H or -CONHC₆H₄CO₂H where
- 10 q is an integer 0 to 5

and salts thereof.

4. Benzoic acid derivatives of the formula (lb)

S XCO₂F

wherein

X represents $CONH(CH_2)_q$, $NHCO(CH_2)_q$ or $O(CH_2)_q$ and

Z represents carboxylic acid, NHSO₂R² or CONHSO₂R², where

R₂ represents C₁-C₄-alkyl or phenyl,

and

q is an integer 1 to 5

and salts thereof.

- 5. Benzoic acid derivatives according to Claim 1 to 4 for therapeutic use.
- 6. A process for the preparation of benzoic acid derivatives according to Claim 1 to 4, characterized in that compounds of the general formula (II)

 $P(CH_2)_mQ$ $T(CH_2)_m-Hal$ (II)

wherein

Hal denotes chlorine, bromine or iodine

are reacted in the presence of an inert solvent, optionally in the presence of a base with compounds of the formula

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$$HX \longrightarrow Y$$
 (III)

and optionally the functional groups Y and Z are transformed by methods known in the art.

- 7. Medicaments containing at least one benzoic acid derivative according to Claim 1 to 4.
- 8. Medicaments according to Claim 7, for the treatment of respiratory diseases.

- 15 9. The use of benzoic acid derivatives according to Claim 1 to 4, for the preparation of medicaments.
 - 10. The use according to Claim 9, for the preparation of medicaments for the treatment of respiratory diseases.